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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,174	11/17/2003	Quan Nguyen	70-000150US	3901

22798 7590 12/16/2005

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,174	NGUYEN ET AL.	
	Examiner	Art Unit	
	Melanie Yu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21-61 and 201-221* is/are pending in the application.

4a) Of the above claim(s) *12,14-17 and 201-221* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13,18,19 and 47-61* is/are rejected.

7)☐ Claim(s) *21-46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/22*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments and amendments filed 22 September 2005 have been entered. Claims 1-19, 21-61 and 201-221 are currently pending in this application. Claims 12, 14-17 and 201-221 have been withdrawn. Claims 20, 62-200 and 222-303 have been canceled. Claims 19, 21, 22, 29, 36, 38 and 59 are currently amended.

Withdrawn Rejections

2. Previous rejections under 35 USC 112, second paragraph have been withdrawn.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 22 September 2005 has been considered by the examiner.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-11, 13 and 18-61 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claims1 and 2, it is unclear whether the first caging groups are considered part of the first state of the substrate. Claims 1 and 2 also recite a substrate for an enzyme, but does not specifically claim an enzyme. It is unclear whether an enzyme is required as part of the composition. If an enzyme is not required as part of the composition, it is unclear how the substrate can be converted into a second state from a first state.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 2 and 57-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Barrett et al. (US 5,252,743).

Barrett et al. teach a composition comprising: a caged sensor comprising: more than one molecule collectively comprising: a substrate for an enzyme, wherein the substrate is in a first station which the enzyme can act, thereby converting the substrate to a second state, wherein the first state is not converted to the second state by cleavage of the enzyme (anti-ligands include substrates for ligands, col. 4, lines 21-54; wherein ligands are enzymes, col. 5, lines 3-11; col. 10, lines 28-37; col. 10, lines 40-63), a first label, wherein a first signal exhibited by the first label is when the substrate is in its first state (first state is unbound with no signal and second state is bound with a signal, col. 21, lines 36-44), and one or more caging groups associated with the a molecule inhibiting an enzyme from acting on a substrate (caged biotin attached to a substrate, col. 4, lines 22-32; col. 9, lines 54-68).

Regarding claims 59 and 60, Barrett et al. teach the caged sensor comprising a first oligonucleotide complementary (ligand is an oligonucleotide, col. 5, lines 3-11) to a second oligonucleotide bound (anti-ligand is an oligonucleotide, col. 4, lines 21-54) to a matrix, which is a surface, at a predetermined location within an array (col. 10, lines 31-35) comprising other oligonucleotides (anti-ligand is bound to a matrix, col. 7, lines 43-54).

Claim Rejections - 35 USC § 103

6. Claims 1-11 and 18 are rejected under 35 USC 103(a) as obvious over Glickman et al. (US 6,806,056) in view of Burbaum et al. (US 5,981,207).

Glickman et al. teach a composition comprising: a cell (the kinase and phosphorylated substrates are in a cell, col. 7, lines 44-48) comprising a sensor for detecting activity of an enzyme comprising: one or more molecules collectively comprising: a substrate for an enzyme (binds tyrosine kinase substrate, col. 2, lines 37-40) wherein the substrate is in a first state on which the enzyme can act, thereby converting the substrate into a second state (first state is prior to phosporylation and second state is after a tyrosine residue has been phosphorylated, col. 4, line 65-col. 5, line 6), and a first label, wherein a first signal is exhibited by the first label when the substrate is in its first state is distinguishable from a second signal exhibited by the first label when the substrate is in its second state (anti-phosphotyrosine antibody is labeled and included in the compositions, col. 5, lines 7-23). Glickman et al. fail to teach one or more first caging groups associated with the one or more molecules.

Burbaum et al. teach a first caging group associated with an enzyme substrate, inhibiting an enzyme from acting upon a substrate (col. 7, lines 36-47), in order to provide a substrate that is initially inactive and can be released into activated form at the appropriate time.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the composition of Glickman et al., a first caging group associated with an enzyme substrate inhibiting the enzyme from acting upon the substrate as taught by Burbaum et al., in order to provide an enzyme substrate that provides rapid and

effective means for detecting and assessing the ability of substances to activate or suppress specific enzyme activity when short lived labels such as alkaline phosphatase are used.

Regarding claims 3-5, the claims are drawn to intended use of a composition and do not appear to require any further physical limitations. Therefore, since all physical limitations required for the composition as recited in claims 1 and 2 are taught by Glickman et al. in view of Burbaum et al., as described above, the composition of Glickman et al. in view of Burbaum et al. is capable of providing the uses recited in claims 3-5.

With respect to claim 6, Glickman et al. teach the first label being an optically detectable label wherein the second signal is a fluorescent signal (col. 11, lines 27-45; col. 9, lines 28-38).

Regarding claims 7-8, Burbaum et al. teach the caging groups being covalently attached to the enzyme substrate, wherein the caging groups are photoliabile and are removed by exposure to light of 366 nm (col. 22, lines 40-55), which is encompassed by the range of between about 60 nm and about 400 nm.

With respect to claims 9-11, Glickman et al. teach the substrate being a polypeptide (protein is with a phosphorylated tyrosine residue, col. 4, line 65-col. 5, line 6), the first label and substrate are physically connected (substrate, protein, is connected to the anti-phosphotyrosine antibody, which is labeled, therefore the fluorescent label and substrate are physically connected, col. 8, lines 9-22) and the substrate comprising one or more amino acids (protein at least contains a tyrosine residue, col. 4, line 65-col. 5, line 6). Glickman et al. also teach a cell comprising a cell lysate (col. 4, line 65-col. 5, line 6).

Regarding claim 18, Glickman et al. teach the enzyme being a protein kinase that phosphorylates tyrosine (col. 8, lines 9-22).

7. Claims 13, 19 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glickman et al. in view of Burbaum et al., as applied to claims 1 and 2, further in view of Kris et al. (US 2003/0096232).

Glickman et al. in view of Burbaum et al., as applied to claims 1 and 2, teach a composition comprising an enzyme substrate, a first label and a first caging group, but fail to teach the substrate being specific for a protease.

Kris et al. teach detection of enzyme activity wherein a substrate is specific for a kinase or a protease (par. 18 and 78), in order to provide a surface that can detect the activity of a plurality of enzymes.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the composition of Glickman et al. in view of Burbaum et al., a protease as the enzyme as taught by Kris et al., in order to identify potential blood thinners or agents which cause blood clots.

Regarding claim 19, Kris et al. also teach a polypeptide substrate (par. 18-19), wherein the one polypeptide comprises a first label and substrate for kinase (labeled antibodies bind to substrate, and therefore a single polypeptide comprises the substrate and first label, par. 256-258), the substrate comprising a tyrosine residue capable of being phosphorylated by the kinase (par. 256), wherein the first label is located at the tyrosine residue and exhibits a first signal when the residue is not phosphorylated and the second signal when the signal is phosphorylated (labels bind to phosphorylated substrates, and therefore bind to the phosphorylated residues, par. 258).

With respect to claim 61, Glickman et al. teach a kit comprising a substrate and a first label (col. 3, lines 16-23). Burbaum et al., as described above, teach a caging group, and Kris et al. teach including instructions for use in a kit (par. 84-87).

8. Claims 47-49 and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glickman et al. in view of Burbaum et al., as applied to claims 1 and 2, further in view of Fischer et al. (Cellular Delivery of Impermeable Effector Molecules in the Form of conjugates with Peptides capable of mediating membrane translocation, 2001, Bioconjugate Chemistry, Vol. 12, No. 6, pages 825-841).

Glickman et al. in view of Burbaum et al., as applied to claims 1 and 2, teach a sensor comprising one or more molecules, but fail to teach the one or more molecules associated with a cellular delivery module.

Fischer et al. teach delivery polypeptide vectors are used to transport entire proteins into a cell (pg. 827, right column, second paragraph), in order to provide delivery of proteins that are longer than a few peptides into a cell.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the substrate of the composition of Glickman et al. in view of Burbaum et al., a cellular delivery module of a polypeptide as taught by Fischer et al., in order to provide in vivo analysis of enzyme activity.

Regarding claim 49, Fischer et al. teach the cellular delivery module covalently attached to the one or more molecules (pg. 825, abstract).

With respect to claims 52-54, Fischer et al. teach that the cellular delivery module can also be used as a sub cellular delivery module by directing the proteins associated with the

module to the same component (pg. 826, right column), in order to provide more accuracy. Fischer et al. teach the sub cellular delivery module being a polypeptide (pg. 827, right column, second paragraph) and covalently attached to the one or more molecules (pg. 825, abstract).

Regarding claims 50, 51, 55 and 56, Burbaum et al. teach covalently attaching a caging group to a polypeptide in order to control activation of the polypeptide (col. 7, lines 37-47).

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include on the cellular delivery modules, a caging group as taught by Burbaum et al., in order to provide control for the time of introduction of the sensor into cellular components.

Response to Arguments

9. Applicant's arguments with respect to claims 2 and 57-60, filed 22 September 2005 have been fully considered but they are not persuasive. With respect to claims 2 and 57-60 applicant argues that Barrett et al. do not suggest use of substrate/enzyme pairs as anti-ligand/ligand pairs on pages 31-32. However, since Barrett et al. teaches an enzyme as a ligand and a substrate as an anti-ligand, Barrett et al. do suggest use of substrate/enzyme pairs. Applicant's further argue that Barrett et al. do not teach one or more caging groups associated with the one or more molecules and inhibiting the enzyme from acting on the substrate. However, according to claim 2, caging compounds are not required to be on the substrate and must only be on the one or more molecules of the caged sensor. Therefore, even if the binding members of Barrett et al. are caged, the caging compounds still performs the intended function of inhibiting an enzyme from acting on the substrate.

10. Previous rejections under 35 USC 112, second paragraph have been withdrawn in light of applicant's amendments and arguments. However, it remains unclear whether the caging group is incorporated into the first or second states of the enzyme substrate. Since the caging group is associated with one or more molecules and inhibits the enzyme from acting upon the substrate, it is unclear whether the caging group is associated with the first state of the enzyme substrate or whether the caging groups are present in the composition while the substrate is in the first and second states.

11. Applicant's arguments with respect to rejections under 35 USC 102(b) and 35 USC 103(a) have been considered but are moot in view of the withdrawal of the rejection under 35 USC 102(b) and 35 USC 103(a) over Fay et al. and in view of the new ground(s) of rejection.

Allowable Subject Matter

12. Claims 21-46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter: the prior art fails to teach a polypeptide substrate for a kinase that comprises a first or second label and one or more first caging groups associated with the polypeptide to inhibit the enzyme from acting on the substrate. Fay et al. teach a polypeptide comprising a substrate for kinase, but fail to teach the polypeptide comprising the first or second label. Burbaum et al. (US 5,981,207) teach a polypeptide comprising a caged enzyme substrate as a probe for detecting an enzyme of alkaline phosphatase. However, Burbaum et al. fail to teach the polypeptide comprising a first or second label and instead the alkaline phosphatase provides a luminescent signal. Craig et al. (US

6,670,144) teach two polypeptides comprising a substrate for kinase wherein one polypeptide comprises a first label and a second polypeptide comprises a second label. Craig et al. fail to teach a single polypeptide comprising a substrate for kinase, a first label and a second label.

Conclusion

Claims 29-46 are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Melanie Yu
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

11/1/07